

U. S. Maine Hosp. Bath. 11
10/27/48

Dear Dr. Hughes,

There is an article "The Clinical Detection of the Genetic Carriers of Inherited Disease" by James V. Neal, Medicine, 26:115-153, 1947, which brings to mind another method of inheritance of the syndrome than "gene-linkage", or the presence of a separate gene for each characteristic on the same chromosome. Neal speaks of pleiotropic genes, or a single gene being responsible for many manifestations. As an example he cites the case of Marfan's disease, or ~~Marfan's~~ Marfan's dactyly, in which a single dominant pleiotropic gene is responsible for the subluxation of the lens, the characteristic elongated body build, congenital heart disease, etc. There is, however, in the same family great variability in the completeness or degree of expression of the individual characteristics due to factors not at all understood. This analogy might seem to make less ~~less~~ puzzling the possibility that some individuals have ~~only~~ only the polyposis of the small intestine and other individuals only the characteristic pigmentation — although, of course, it doesn't explain it.

Genetically the Syndrome is analogous to amaurotic family idiocy or ~~but~~ hereditary optic atrophy in which the patient is not born with the characteristics but only develops them as he ages.

James Harold Saint, "Polypsi of the Intestines", Brit. J. of Surgery 15:99-119, 1927, gives a ratio of 4:1 as the approximate incidence of polyposis in the large intestine as compared with that in the small int.

I have found the following reports of familial adenomatosis of the small intestine. The reports are too skimpy to permit construction of any sort of genealogical chart.

① William H. Haggard and William O. Floyd, "Repeated Recurrences for Intussusception Due to Familial Tumors of the Small Intestine," *Am. J. Surg.* 28: 428-438, 1935.

The father had 4 operations, 3 for intussusception and 1 for malignant degeneration. A daughter had 2 operations for intussusception due to adenomatous polyp. A son had 3 operations for the same reason.

② Van Disk, J. A., and Oordendal, A. J. F., "Adenoom van den Dunnen Darm," *Nederl. Tijdsch. v. Geneesk.*, *Ams.*, 1925, LXIX, 966-973.

A brother and sister both had several operations within a ^{relatively} short time for intussusception due to many adenomata of the upper ileum.

Sincerely,
Victor A. McKusick